

LETTERS TO THE EDITORS

Ciclesonide as a manic trigger in a patient with long-term stable bipolar disorder: a case report

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Adverse effects are frequent during systemic corticosteroid therapy, with the most common psychiatric effects being hypomania and mania.¹ Nasal corticosteroids may also have psychiatric effects. In addition to dose- and time-dependent risks, the incidence of psychiatric adverse effects may differ across different intranasal corticosteroid preparations and individual patients. However, whether a history of psychiatric disorder exacerbates the risk of adverse psychiatric reactions during corticosteroid therapy remains unclear.^{1,2}

To the best of our knowledge, this is the first report of an episode of mania triggered by the use of ciclesonide in a patient with bipolar disorder (BD). To date, the triggering of manic symptoms by steroid nasal sprays in patients with BD has been described in only two case reports.^{2,3}

A 51-year-old married male dentist was diagnosed with BD 24 years prior to the event reported here. The natural history of the disease was characterized by depressive episodes, hypomanic episodes, and manic episodes with psychotic features, which were resistant to first- and second-line treatments, such as mood stabilizers and some second-generation antipsychotics. After several drug trials, optimal results were obtained using a combination of clozapine (100-150 mg/day) and fluvoxamine (100-250 mg/day), which he took for 17 years. During this period, he experienced only minor mood fluctuations, which were primarily attributed to life events.

In addition to his psychiatric disorders, he had chronic allergic rhinitis, which was primarily treated with montelukast and occasionally with antihistamines and low-dosage intranasal corticosteroids. He generally avoided corticosteroids, even at low doses, because they triggered transient subthreshold depressive symptoms and/or dysphoria.

For 2 years, he had been mostly well, with only transient subsyndromal depressive symptoms, until he experienced a severe bout of rhinitis accompanied by poor sleep, which was triggered by exposure to mold in a hostel. Six days after the rhinitis bout, he was prescribed ciclesonide

(200 µg/day) for the first time. After 4 days of use, he experienced fluctuating manic symptoms, manifested by irritability, excitement, lability, amplified energy, inflated self-esteem, decreased need for sleep, pressure to keep talking, minor derailment, occasional fleeting delusions with themes of grandiosity, and paranoia. These symptoms were associated with impairment in social and occupational functioning. Approximately 10 days after the onset of the manic symptoms, he had a psychiatric consultation at our clinic and was advised to discontinue the use of ciclesonide, and an increased dose of clozapine was prescribed. Two days after ciclesonide discontinuation, all symptoms disappeared, and clozapine was decreased to the usual dose. During a 2.5-year follow-up period, the patient reported feeling well, with only minor and brief mood fluctuations, without repercussions in his conjugal, social, or professional life.

Intranasally administered corticosteroids exhibit a good safety profile, especially the new-generation drugs in this class, such as ciclesonide, fluticasone, and mometasone. Ciclesonide, a prodrug that is activated locally in the airway mucosa, is considered to be the safest intranasally administered corticosteroid.¹ Although the drug label reports symptoms of depression as one of the side effects of its nasal administration, other psychiatric symptoms remain unreported.⁴

We hypothesize that ciclesonide triggered the manic episode in our patient. Prior to ciclesonide administration, he had been stable for 2 years. He displayed good treatment adherence, did not use illicit drugs or alcohol, and had not experienced any significant life event. Since discontinuation of ciclesonide, the patient has remained asymptomatic for 2.5 years.

The two previous case reports of manic episodes triggered by intranasal steroids involved the use of beclometasone and mometasone by women aged 28 and 53 years, respectively.^{2,3} The first patient needed to be hospitalized for 2.5 weeks to receive antipsychotic and mood-stabilizer therapy. The condition of the second patient improved spontaneously within a few days of corticosteroid discontinuation. In the case reported herein, we decided to discontinue corticosteroid therapy and increase the dose of the antipsychotic agent because the course and treatment of intranasal corticosteroid-precipitated manic episodes in patients with BD are not well established. Sleep impairment, which can trigger mood-fluctuation episodes in patients with BD, is another aspect that is worth considering; in this case, it may be attributed to allergic sinusitis.⁵

This case report suggests that intranasal ciclesonide therapy can trigger manic episodes in patients with BD. Moreover, allergic sinusitis-related sleep problems may be a risk factor for manic episodes. Hence, psychiatrists should educate patients and their family members about the risks of intranasal corticosteroids.

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Disclosure

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Alcohol misuse by Amerindians with tuberculosis: relations to cash transfer programs in Brazil

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Alcohol misuse is a remarkable risk factor for tuberculosis (TB) and limits access to health services and adherence to medications, especially among socioeconomically disadvantaged populations, such as indigenous people.¹ Minimum-income public policies, specifically cash transfer programs (CTPs), have been adopted to improve the social and health indicators of these groups in several countries.²

We conducted a cross-sectional study among Guarani-Kaiowá villages in the state of Mato Grosso do Sul, Brazil, between 2011-2016. Our purpose was to estimate the

prevalence of alcohol misuse by indigenous Brazilians undergoing TB treatment and its association with CTPs granted by the Brazilian federal government. Sex, age, place of residence, educational attainment, severity of TB, and CTP were the variables of interest. The study was approved by the research ethics committee of Escola Nacional de Saúde Pública Sergio Arouca (protocol 96/2010) and by the Brazilian National Ethics Commission (protocol 400/2010).

Alcohol misuse was defined as an Alcohol Use Disorders Identification score higher than 8 points for men or 7 for women. In this study, families were considered CTP recipients when they received either rural retirement benefits, the Bolsa Família program, or both. The purpose of the Bolsa Família program is to immediately alleviate poverty in families that are proven to be vulnerable, who commit to conditionalities related to education and health care. To estimate the prevalence ratio, we used the Poisson regression.

Overall, 197 TB cases were reported during the period. Of these, 35.5% (confidence interval: 28.8-42.2) exhibited alcohol misuse. On average, alcohol misuse was 50% (prevalence ratio: 1.5; confidence interval: 1.1-2.0) more frequent in individuals whose families did not have access to CTPs (Table 1).

The prevalence of alcohol misuse among indigenous people undergoing TB treatment in this sample was close to that observed in TB patients from India (38.8%),³ as well in admittedly vulnerable groups, such as homeless and transgender individuals.¹

The inverse association between CTPs and alcohol misuse in indigenous people, as shown here, occurs in a context marked by precarious housing, low education and income levels, and food insecurity.⁴ We believe the majority of the indigenous population living in the investigated villages would meet the criteria to receive at least one of the CTPs here investigated. However, recent studies^{4,5} revealed that these especially vulnerable groups have faced major difficulties in accessing CTPs in Brazil.

Even if access to CTPs does not ensure protection against alcohol misuse, our data show that individuals undergoing TB treatment and suffering from alcohol misuse, and thus bearing a double burden of vulnerability, were more likely to not have access to CTPs. Despite meeting the criteria and being eligible, part of these individuals had limited access to CTPs and/or faced troubles remaining enrolled in the social programs.

In settings of great socioeconomic vulnerability, such as among indigenous people in Mato Grosso do Sul state, people who should have access to CTPs but who, for various reasons, are unable to achieve access or remain enrolled in these programs should receive special attention, not only from social security and social assistance but also from the health authorities. Limiting the access of these individuals to CTPs seems inadequate from a public health viewpoint, since it can deepen social inequalities as well hinder tuberculosis control among indigenous people.